10/542,003

search w/ enzyme

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*                                                          *
*     CASREACT now has more than 10 million reactions      *
*                                                          *
************************************************************
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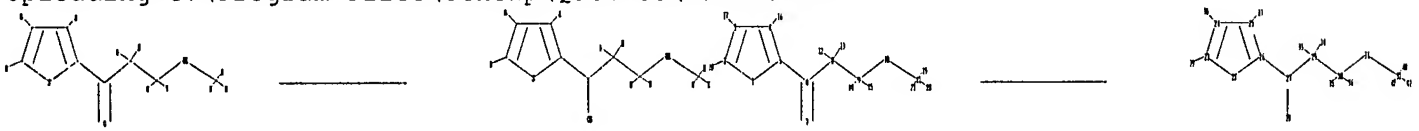
Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
Uploading C:\Program Files\Stnexp\Queries\Karen3.str



chain nodes :
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 27 28 29 30 31 32 33
34 35 36 37 38 39 40 41 42
ring nodes :
1 2 3 4 5 22 23 24 25 26
chain bonds :
2-18 3-17 4-16 5-6 6-7 6-8 8-9 8-12 8-13 9-10 9-14 9-15 10-11 11-19 11-20
11-21 23-39 24-38 25-37 26-27 27-29 27-28 29-30 29-33 29-34 30-31 30-35 30-36
31-32 32-40 32-41 32-42
ring bonds :
1-2 1-5 2-3 3-4 4-5 22-23 22-26 23-24 24-25 25-26
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 9-10 10-11 22-23 22-26 23-24 24-25 25-26 27-28 30-31
31-32
exact bonds :
2-18 3-17 4-16 5-6 6-7 6-8 8-9 8-12 8-13 9-14 9-15 11-19 11-20 11-21 23-39
24-38 25-37 26-27 27-29 29-30 29-33 29-34 30-35 30-36 32-40 32-41 32-42

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:CLASS 28:CLASS
29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS
38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS

L4 STRUCTURE UPLOADED

=> s l4 ful
FULL SEARCH INITIATED 14:33:18 FILE 'CASREACT'
SCREENING COMPLETE - 1512 REACTIONS TO VERIFY FROM 270 DOCUMENTS

100.0% DONE 1512 VERIFIED 22 HIT RXNS 8 DOCS
SEARCH TIME: 00.00.01

L5 8 SEA SSS FUL L4 (22 REACTIONS)

10/5/2006

```
=> s l5 and (enzyme or microbial or dehydrogenase or enantioselective or catalyst)
         10805 ENZYME
          2788 MICROBIAL
          1375 DEHYDROGENASE
         12257 ENANTIOSELECTIVE
         81437 CATALYST
L6           6 L5 AND (ENZYME OR MICROBIAL OR DEHYDROGENASE OR ENANTIOSELECTIVE
               OR CATALYST)

=> d ibib abs hit 1-6
```

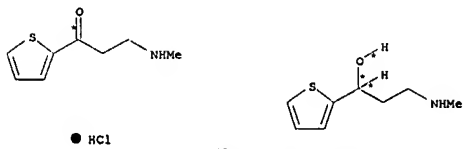
L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 143:248273 CASREACT
TITLE: Preparation of enantiomerically pure 1-substituted-3-amino alcohols
INVENTOR(S): Michel, Dominique
PATENT ASSIGNEE(S): Lonza A.-G., Switz.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1566383	A1	20050824	EP 2004-3809	20040219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
WO 2005080370	A1	20050901	WO 2005-EP1781	20050221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			EP 2004-3809	20040219
			EP 2004-10043	20040428

OTHER SOURCE(S): MARPAT 143:248273
AB Provided is a process for the preparation of enantiomerically pure 1-substituted-3-amino alcs. (R)- or (S)-HOCH(R1)CH2CH2NHR2 (R1 = 2-thienyl, 2-furanyl, Ph, substituted 2-thienyl, substituted 2-furanyl, substituted Ph; R2 = C1-C4-alkyl, Ph, substituted C1-C4-alkyl, substituted Ph), particularly (S)-(-)- and (R)-(+)-3-N-methylamino-1-(2-thienyl)-1-propanol, by asym. hydrogenating salts of R1COCH2CH2NHR2 using Rh and an asym. ligand.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(2) OF 31 ...D ===> F

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)



D (2) ⟹ F YIELD 84%

RX(2) RCT D 645411-16-1

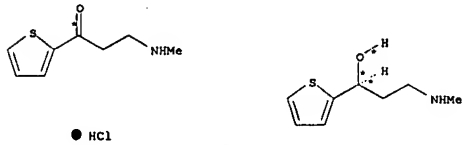
STAGE(1)
RGT G 1310-73-2 NaOH
SOL 7732-18-5 Water, 64-17-5 EtOH
CON 5 minutes, 4 deg C

STAGE(2)
RGT H 16940-66-2 NaBH4
CON SUBSTAGE(1) 30 minutes, 4 deg C
SUBSTAGE(2) 4 hours, 4 deg C

STAGE(3)
RGT I 67-64-1 Me2CO
CON SUBSTAGE(1) 5 minutes
SUBSTAGE(2) 10 minutes

PRO F 116539-56-1
NTE incremental addition of sodium borohydride in second stage

RX(3) OF 31 ...D ===> K



D (3) ⟹ K YIELD 92%

RX(3) RCT D 645411-16-1

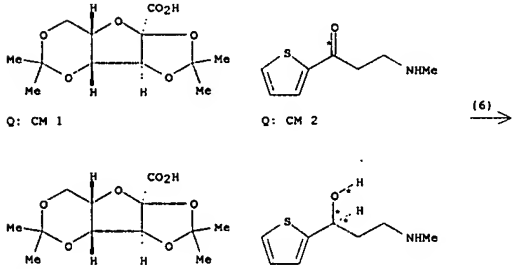
STAGE(1)
RGT G 1310-73-2 NaOH
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 50 deg C

STAGE(3)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

PRO K 116539-55-0
NTE [Rh((S,S)-Me-Duphos)]BF4 used as catalyst stage 2, stereoselective, autoclave used, high pressure in last stage, ee = 97%, optimized on catalyst

RX(6) OF 31 ...Q ===> N...



Q: CM 1 Q: CM 2 (6) ⟹ N: CM 1 N: CM 2

RX(6) RCT Q 863094-06-8

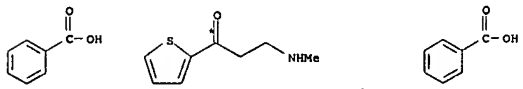
STAGE(1)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature
SUBSTAGE(3) room temperature -> 50 deg C

STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

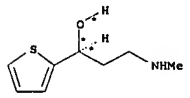
PRO N 569687-76-9

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
NTE [Rh((R,R,S,S)-tangphos)(norbornadiene)]BF4 used as catalyst stage 1, stereoselective, high pressure in last stage, autoclave used, ee = 95%, conversion is 100%

RX(9) OF 31 ...V ===> W



V: CM 1 V: CM 2 (9) ⟹ W: CM 1



W: CM 2

RX(9) RCT V 863094-15-9

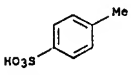
STAGE(1)
CAT 205064-10-4 Rhodium(1+), [(1,2,5,6-η)-1,5-cyclooctadiene][(2S,2'S,5S,5'S)-1,1'-(1,2-phenylene)bis[2,5-dimethylphospholane-κP]]-, tetrafluoroborate(1-)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 50 deg C

STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

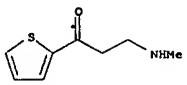
PRO W 863094-19-3
NTE stereoselective, high pressure in last stage, autoclave used, ee = 96.7%, conversion is 99%

RX(11) OF 31 ...Z ===> AA

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)

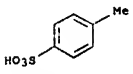


Z: CM 1

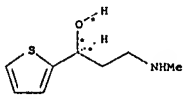


Z: CM 2

(11)



AA: CM 1



AA: CM 2

RX(11) RCT Z 863094-23-9

STAGE(1)
CAT 205064-10-4 Rhodium(1+), [(1,2,5,6-η)-1,5-cyclooctadiene][(2S,2'S,5S,5'S)-1,1'-(1,2-phenylene)bis[2,5-dimethylphospholane-κP]]-, tetrafluoroborate(1-)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 50 deg C

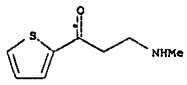
STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

PRO AA 863094-27-3
NTE stereoselective, high pressure in last stage, autoclave used, ee = 90%, conversion is 5%

RX(13) OF 31 ...AC ===> AD

$HO_2C-(CH_2)_{10}-Me$

AC: CM 1

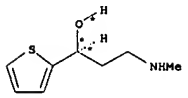


AC: CM 2

(13)

$HO_2C-(CH_2)_{10}-Me$

AD: CM 1



AD: CM 2

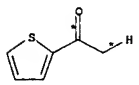
RX(13) RCT AC 863094-31-9

STAGE(1)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 50 deg C

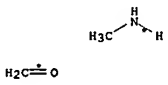
STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

PRO AD 863094-35-3
NTE stereoselective, high pressure in last stage, autoclave used, ee = 93.6%, conversion is 100%

RX(15) OF 31 COMPOSED OF RX(1), RX(3)
RX(15) A + B + C ===> K



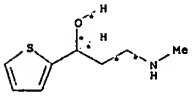
A



B C

● HCl

2 STEPS



K
YIELD 92%

RX(1) RCT A 88-15-3, B 50-00-0, C 593-51-1
PRO D 645411-16-1
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 9 hours, 120 - 130 deg C
SUBSTAGE(2) 130 deg C -> 20 deg C
NTE paraformaldehyde used, autoclave used

RX(3) RCT D 645411-16-1

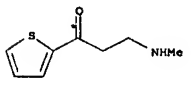
STAGE(1)
RGT G 1310-73-2 NaOH
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 50 deg C

STAGE(3)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

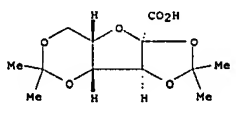
PRO K 116539-55-0
NTE [Rh((S,S)-Me-Duphos)]BF4 used as catalyst stage 2, stereoselective, autoclave used, high pressure in last stage, ee = 97%, optimized on catalyst

RX(21) OF 31 COMPOSED OF RX(5), RX(6)
RX(21) D + P ===> N



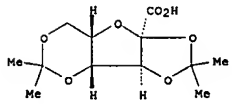
● HCl

D

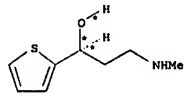


P

2 STEPS



N: CM 1



N: CM 2

RX(5) RCT D 645411-16-1

STAGE(1)
RGT G 1310-73-2 NaOH
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 15 minutes, 0 deg C
SUBSTAGE(3) 10 minutes, 0 deg C

STAGE(2)
RCT P 18467-77-1
SOL 1634-04-4 t-BuOMe
CON room temperature

PRO Q 863094-06-8
NTE scalable

RX(6) RCT Q 863094-06-8

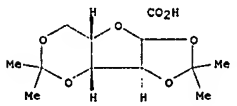
STAGE(1)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature
SUBSTAGE(3) room temperature -> 50 deg C

STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

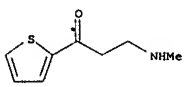
PRO N 569687-76-9
NTE [Rh((R,R,S,S)-tangphos)(norbornadiene)]BF4 used as catalyst stage 1, stereoselective, high pressure in last stage, autoclave used, ee = 95%, conversion is 100%

RX(22) OF 31 COMPOSED OF RX(6), RX(4)
RX(22) Q ===> K

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)

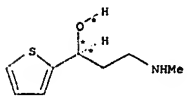


Q: CM 1



Q: CM 2

2 STEPS



K
YIELD 87%

RX(6) RCT Q 863094-06-8

STAGE(1)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature
SUBSTAGE(3) room temperature -> 50 deg C

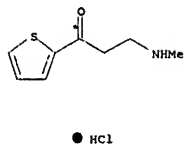
STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

PRO N 569687-76-9
NTE [Rh((R,R,S,S)-tangphos)(norbornadiene)]BF4 used as catalyst stage 1, stereoselective, high pressure in last stage, autoclave used, ee = 95%, conversion is 100%

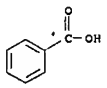
RX(4) RCT N 569687-76-9
RGT G 1310-73-2 NaOH
PRO K 116539-55-0
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 15 minutes, room temperature
NTE incrmental addition of reactant

RX(23) OF 31 COMPOSED OF RX(8), RX(9)
RX(23) D + U ===> W

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)

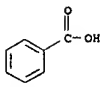


D

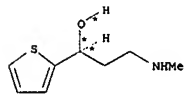


U

2 STEPS



W: CM 1



W: CM 2

RX(8) RCT D 645411-16-1

STAGE(1)
RGT G 1310-73-2 NaOH
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe
CON SUBSTAGE(1) room temperature -> 10 deg C
SUBSTAGE(2) 5 - 10 deg C
SUBSTAGE(3) 15 minutes, 5 - 10 deg C

STAGE(2)
RCT U 65-85-0
SOL 1634-04-4 t-BuOMe
CON 15 minutes, <10 deg C

PRO V 863094-15-9

RX(9) RCT V 863094-15-9

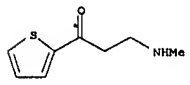
STAGE(1)
CAT 205064-10-4 Rhodium(1+), [(1,2,5,6-η)-1,5-cyclooctadiene][(2S,2'S,5S,5'S)-1,1'-(1,2-phenylene)bis[2,5-dimethylphospholane-κP]]-, tetrafluoroborate(1-)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 50 deg C

STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C

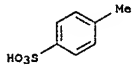
L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
SUBSTAGE(3) 50 deg C -> room temperature

PRO W 863094-19-3
NTE stereoselective, high pressure in last stage, autoclave used, ee = 96.7%, conversion is 99%

RX(24) OF 31 COMPOSED OF RX(10), RX(11)
RX(24) D + Y ===> AA

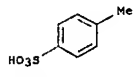


D

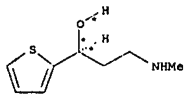


Y

2 STEPS



AA: CM 1



AA: CM 2

RX(10) RCT D 645411-16-1

STAGE(1)
RGT G 1310-73-2 NaOH
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe
CON SUBSTAGE(1) room temperature -> 10 deg C
SUBSTAGE(2) 5 - 10 deg C
SUBSTAGE(3) 15 minutes, 5 - 10 deg C

STAGE(2)
RCT Y 104-15-4
SOL 1634-04-4 t-BuOMe
CON 15 minutes, <10 deg C

PRO Z 863094-23-9

RX(11) RCT Z 863094-23-9

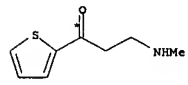
STAGE(1)
CAT 205064-10-4 Rhodium(1+), [(1,2,5,6-η)-1,5-cyclooctadiene][(2S,2'S,5S,5'S)-1,1'-(1,2-phenylene)bis[2,5-dimethylphospholane-κP]]-, tetrafluoroborate(1-)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
SUBSTAGE(2) room temperature -> 50 deg C

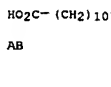
STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

PRO AA 863094-27-3
NTE stereoselective, high pressure in last stage, autoclave used, ee = 90%, conversion is 5%

RX(25) OF 31 COMPOSED OF RX(12), RX(13)
RX(25) D + AB ===> AD



D

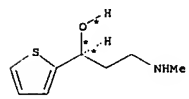


AB

2 STEPS

$HO_2C-(CH_2)_{10}-Me$

AD: CM 1



AD: CM 2

RX(12) RCT D 645411-16-1

STAGE(1)
RGT G 1310-73-2 NaOH
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe
CON SUBSTAGE(1) room temperature -> 10 deg C
SUBSTAGE(2) 5 - 10 deg C
SUBSTAGE(3) 15 minutes, 5 - 10 deg C

STAGE(2)
RCT AB 143-07-7
SOL 1634-04-4 t-BuOMe

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
CON SUBSTAGE(1) 15 minutes, <10 deg C
SUBSTAGE(2) 1 hour

PRO AC 863094-31-9

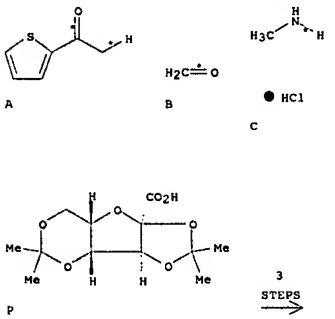
RX(13) RCT AC 863094-31-9

STAGE(1)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 50 deg C

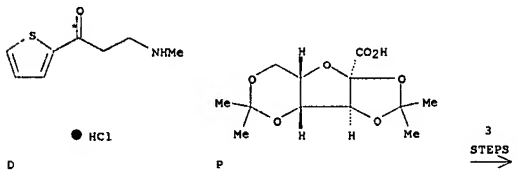
STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

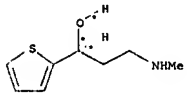
PRO AD 863094-35-3
NTE stereoselective, high pressure in last stage, autoclave used, ee = 93.6%, conversion is 100%

RX(26) OF 31 COMPOSED OF RX(1), RX(5), RX(6)
RX(26) A + B + C + P ===> N



L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
RX(30) D + P ===> K





YIELD 87%

RX(5) RCT D 645411-16-1

STAGE(1)
RGT G 1310-73-2 NaOH
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 15 minutes, 0 deg C
SUBSTAGE(3) 10 minutes, 0 deg C

STAGE(2)
RCT P 18467-77-1
SOL 1634-04-4 t-BuOMe
CON room temperature

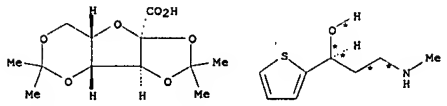
PRO Q 863094-06-8
NTE scalable

RX(6) RCT Q 863094-06-8

STAGE(1)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature
SUBSTAGE(3) room temperature -> 50 deg C

STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)



RX(1) RCT A 88-15-3, B 50-00-0, C 593-51-1
PRO D 645411-16-1
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 9 hours, 120 - 130 deg C
SUBSTAGE(2) 130 deg C -> 20 deg C
NTE paraformaldehyde used, autoclave used

RX(5) RCT D 645411-16-1

STAGE(1)
RGT G 1310-73-2 NaOH
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 15 minutes, 0 deg C
SUBSTAGE(3) 10 minutes, 0 deg C

STAGE(2)
RCT P 18467-77-1
SOL 1634-04-4 t-BuOMe
CON room temperature

PRO Q 863094-06-8
NTE scalable

RX(6) RCT Q 863094-06-8

STAGE(1)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature
SUBSTAGE(3) room temperature -> 50 deg C

STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

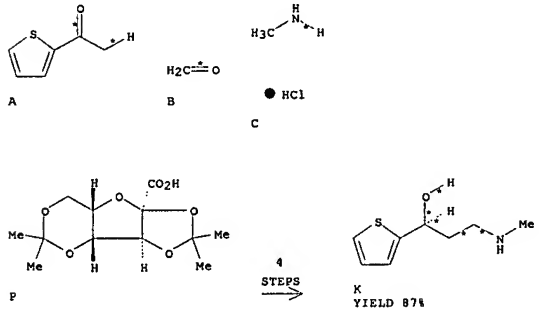
PRO N 569687-76-9
NTE [Rh((R,R,S,S)-tangphos)(norbornadiene)]BF4 used as catalyst stage 1, stereoselective, high pressure in last stage, autoclave used, ee = 95%, conversion is 100%

RX(30) OF 31 COMPOSED OF RX(5), RX(6), RX(4)

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
PRO N 569687-76-9
NTE [Rh((R,R,S,S)-tangphos)(norbornadiene)]BF4 used as catalyst stage 1, stereoselective, high pressure in last stage, autoclave used, ee = 95%, conversion is 100%

RX(4) RCT N 569687-76-9
RGT G 1310-73-2 NaOH
PRO K 116539-55-0
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 15 minutes, room temperature
NTE incrmental addition of reactant

RX(31) OF 31 COMPOSED OF RX(1), RX(5), RX(6), RX(4)
RX(31) A + B + C + P ===> K



YIELD 87%

RX(1) RCT A 88-15-3, B 50-00-0, C 593-51-1
PRO D 645411-16-1
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 9 hours, 120 - 130 deg C
SUBSTAGE(2) 130 deg C -> 20 deg C
NTE paraformaldehyde used, autoclave used

RX(5) RCT D 645411-16-1

STAGE(1)
RGT G 1310-73-2 NaOH
SOL 7732-18-5 Water, 1634-04-4 t-BuOMe
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 15 minutes, 0 deg C
SUBSTAGE(3) 10 minutes, 0 deg C

STAGE(2)
RCT P 18467-77-1
SOL 1634-04-4 t-BuOMe

L6 ANSWER 1 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
CON room temperature

PRO Q 863094-06-8
NTE scalable

RX(6) RCT Q 863094-06-8

STAGE(1)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature
SUBSTAGE(3) room temperature -> 50 deg C

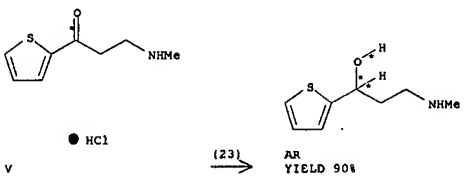
STAGE(2)
RGT L 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 30 bar
SUBSTAGE(2) 5 hours, 50 deg C
SUBSTAGE(3) 50 deg C -> room temperature

PRO N 569687-76-9
NTE [Rh((R,R,S,S)-tangphos)(norbornadiene)]BF4 used as catalyst stage 1, stereoselective, high pressure in last stage, autoclave used, ee = 95%, conversion is 100%

RX(4) RCT N 569687-76-9
RGT G 1310-73-2 NaOH
PRO K 116539-55-0
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 15 minutes, room temperature
NTE incremental addition of reactant

L6 ANSWER 2 OF 6 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:481782 CASREACT
TITLE: Practical synthesis of enantiopure γ-amino alcohols by rhodium-catalyzed asymmetric hydrogenation of β-secondary-amino ketones
AUTHOR(S): Liu, Duan; Gao, Wenzhong; Wang, Chunjiang; Zhang, Xumu
CORPORATE SOURCE: Department of Chemistry, The Pennsylvania State University, University Park, PA, 16802, USA
SOURCE: Angewandte Chemie, International Edition (2005), 44(11), 1687-1689
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several β-secondary amino ketone hydrochlorides were hydrogenated with remarkably high enantioselectivities by using a rhodium complex containing P-chiral bisphospholane. These results establish a short and practical means for the synthesis of enantiopure N-monosubstituted γ-amino alcs., which are key intermediates in the synthesis of important antidepressants. For example, the bis[di(methyl)ethyl]tetra(hydro)-1,1'-bi-1H-isophosphindole-rhodium-catalyzed stereoselective hydrogenation of 3-(methylamino)-1-phenyl-1-propanone hydrochloride gave (αS)-α-[2-[(methyl)amino]ethyl]benzenemethanol, which is a synthetic precursor for (γS)-N-methyl-γ-[4-(trifluoromethyl)phenoxy]benzenepropanamine [i.e., (S)-fluoxetine]. The synthesis of (αS)-[-[(methyl)amino]ethyl]thiophenemethanol, a key synthetic intermediate for (S)-duloxetine, was also reported.

RX(23) OF 74 ...V ===> AR



V —(23)→ AR, YIELD 90%

RX(23) RCT V 645411-16-1

STAGE(1)
RGT Z 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1 hour, room temperature

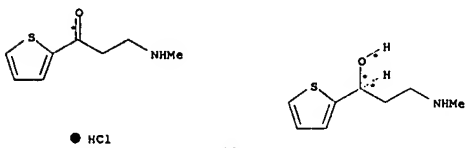
STAGE(2)
RGT AA 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

L6 ANSWER 2 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)

STAGE(3)
RGT AB 1310-73-2 NaOH
SOL 7732-18-5 Water
CON room temperature, basify

PRO AR 116539-56-1

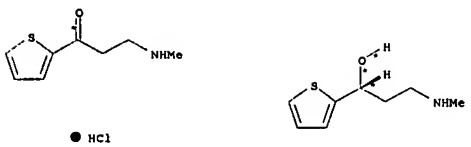
RX(33) OF 74 ...V ===> BE...



V —(33)→ BE, YIELD 93%

RX(33) RCT V 645411-16-1
RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2
PRO BE 116539-55-0
CAT 851936-69-1 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1S,1'S,2S,2'S)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)
SOL 67-56-1 MeOH
CON 12 hours, 50 deg C, 10 bar
NTE stereoselective

RX(34) OF 74 ...V ===> BF



V —(34)→ BF, YIELD 93%

RX(34) RCT V 645411-16-1
RGT AV 584-08-7 K2CO3, AW 1333-74-0 H2
PRO BF 116539-57-2
CAT 850780-91-5 Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene][(1R,1'R,2R,2'R)-2,2'-bis(1,1-dimethylethyl)-2,2',3,3'-tetrahydro-1,1'-bi-1H-isophosphindole-κP2,κP2']-, (OC-6-11)-hexafluoroantimonate(1-)

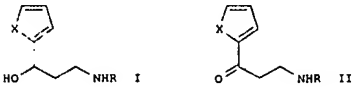
L6 ANSWER 2 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
SOL 67-56-1 MeOH
CON 12 hours, 50 deg C, 10 bar
NTE stereoselective

IT 850780-91-5 851936-69-1
RL: CAT (Catalyst use); USES (Uses)
(preparation of chiral γ-amino alc. derivs. by stereoselective hydrogenation of β-secondary amino ketone derivs. using chiral bis[di(methyl)ethyl]tetra(hydro)-1,1'-bi-1H-isophosphindole-rhodium as catalyst)

L6 ANSWER 3 OF 6 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:280046 CASREACT
TITLE: Process for the asymmetric hydrogenation of β-amino ketones using transition metal complexes of chiral bidentate phosphines as catalysts.
PATENT ASSIGNEE(S): Lonza AG, Switz.
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1510517	A1	20050302	EP 2003-77734	20030901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004268057	A1	20050310	AU 2004-268057	20040831
WO 2005021527	A2	20050310	WO 2004-EP9690	20040831
WO 2005021527	A3	20050714		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1664014	A2	20060607	EP 2004-764655	20040831
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
NO 2006000763	A	20060317	NO 2006-763	20060217
PRIORITY APPLN. INFO.:			EP 2003-77734	20030901
			WO 2004-EP9690	20040831

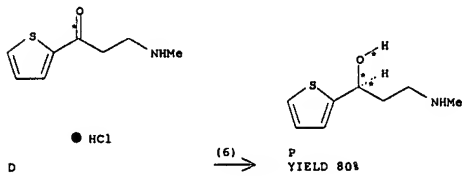
OTHER SOURCE(S): MARPAT 142:280046
GI



AB A process for the preparation of enantiomerically enriched or enantiomerically pure β-amino alcs. [I; X = S, O; R = (substituted) alkyl, cycloalkyl, aryl, aralkyl] comprises asym. hydrogenation of ketones (II; variables as above) using transition metal complexes of chiral bidentate phosphines as catalysts. Thus, 3-methylamino-1-(thien-2-yl)propan-1-one hydrochloride (preparation given), NaOMe, (S,S)-Me-DuPhos, and [Rh(COD)2]BF4 were autoclaved

L6 ANSWER 3 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
together in MeOH at 30-34° and 30 bar H2 for 5 h to give 67% (S)-3-methylamino-1-(2-thienyl)-1-propanol in >99% enantiomeric excess.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(6) OF 7 ...D ===> P



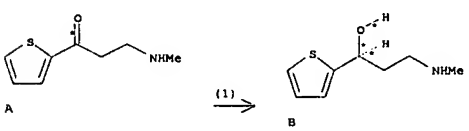
RX(6) RCT D 645411-16-1
RGT Q 124-41-4 NaOMe, R 1333-74-0 H2
PRO P 116539-55-0
CAT 248244-33-9 5H-Phospholo[3,4-d]-1,3-dioxole, 5,5'-(1,2-phenylene)bis[tetrahydro-2,2,4,6-tetramethyl-, (3aS,3'aS,4S,4'S,6S,6'S,6aS,6'aS)-, 35138-22-8 Rhodium(1+), bis[(1,2,5,6-η)-1,5-cyclooctadiene]-, tetrafluoroborate(1-)
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 24 hours, 30 - 70 deg C, 30 bar
NTE high pressure, optimization study, stereoselective
ST aminoketone asym hydrogenation ruthenium rhodium chiral bidentate phosphine catalyst; aminoalc chiral prepn; aminothienylpropanone aminofurylpropanone asym hydrogenation; thienylaminoalc furylaminoalc chiral prepn

L6 ANSWER 4 OF 6 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:348875 CASREACT
TITLE: L-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in production of substituted (S)-alkanols
INVENTOR(S): Althoefer, Henning; Kesseler, Maria
PATENT ASSIGNEE(S): BASF A.-G., Germany
SOURCE: Ger. Offen., 41 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10315760	A1	20041021	DE 2003-10315760	20030407
CA 2521288	AA	20041021	CA 2004-2521288	20040406
WO 2004090094	A2	20041021	WO 2004-EP3655	20040406
WO 2004090094	A3	20050317		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1613745	A2	20060111	EP 2004-725924	20040406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1771323	A	20060510	CN 2004-80009243	20040406
JP 2006521800	T2	20060928	JP 2006-505019	20040406
US 2006211099	A1	20060921	US 2005-552218	20051006
PRIORITY APPLN. INFO.:			DE 2003-10315760	20030407
			WO 2004-EP3655	20040406

AB The present invention concerns proteins, which possess an enzymic activity for reduction of substituted alkanones, such as 3-methylamino-1-(2-thienyl)-propane-1-one. Furthermore, the invention concerns nucleic acids which code for these proteins, vectors, and genetically modified microorganisms as well as procedures for the production of substituted (S)-alkanols, e.g., (S)-3-methylamino-1-(2-thienyl)-(S)-propanol. This compound may be used in the synthesis of duloxetine.

RX(1) OF 1 A ===> B



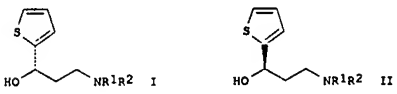
L6 ANSWER 4 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
RX(1) RCT A 667465-15-8
PRO B 116539-55-0
SOL 7732-18-5 Water
CON 1 - 23 hour, 30 deg C, pH 7
NTE biotransformation, described medium, enzymic, stereoselective, Tris-HCl buffered solution used, carntine or hydroxyacyl-CoA-dehydrogenase used
TI L-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in production of substituted (S)-alkanols
ST carnitine dehydrogenase alkanone redn chiral alkanol duloxetine synthesis
IT Alcohols, preparation
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(chiral; l-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in production of substituted (S)-alkanols)
IT Agrobacterium
Agrobacterium tumefaciens
Alcaligenes
Archaeoglobus
Archaeoglobus fulgidus
Enterobacteriaceae
Mesorhizobium loti
Molecular cloning
Nocardiaceae
Pseudomonadaceae
Pseudomonas
Pseudomonas aeruginosa
Pseudomonas putida
Rhizobiaceae
Rhizobium
Staphylococcus
Staphylococcus epidermidis
Streptomyces
Streptomyces coelicolor
Streptomycetaceae
Xanthomonas
Xanthomonas campestris
(l-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in production of substituted (S)-alkanols)
IT 775366-21-7, Dehydrogenase, carnitine (Alcaligenes) 775366-22-8 775366-23-9 775366-24-0 775366-25-1 775366-26-2 775366-27-3 775366-28-4 775366-29-5
RL: CAT (Catalyst use); PRP (Properties); USES (Uses)
(amino acid sequence; l-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in production of substituted (S)-alkanols)
IT 116539-55-0P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(l-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in production of substituted (S)-alkanols)
IT 9028-40-4, E.c. 1.1.1.35 9045-45-8, E.c. 1.1.1.108
RL: CAT (Catalyst use); USES (Uses)
(l-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in production of substituted (S)-alkanols)
IT 667465-15-8

L6 ANSWER 4 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
RL: RCT (Reactant); RACT (Reactant or reagent)
(l-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in prodn. of substituted (S)-alkanols)
IT 116539-59-4P, Duloxetine
RL: SPN (Synthetic preparation); PREP (Preparation)
(l-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in production of substituted (S)-alkanols)
IT 775366-20-6
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; l-carnitine dehydrogenase and microorganisms producing L-carnitine dehydrogenase and their use in production of substituted (S)-alkanols)

L6 ANSWER 5 OF 6 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:321232 CASREACT
TITLE: Preparation of optically active 3-amino-1-(2-thienyl)-1-propanols via reduction of 3-amino-1-(2-thienyl)-1-propanones using a hydrogen donor in the presence of a metal catalyst, an optically active nitrogen-containing ligand and optionally a base.
INVENTOR(S): Fuchs, Rudolf; Michel, Dominique; Brieden, Walter
PATENT ASSIGNEE(S): Lonza A.-G., Switz.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004031168	A2	20040415	WO 2003-EP11073	20031007
WO 2004031168	A3	20040826		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003276066	A1	20040423	AU 2003-276066	20031007
PRIORITY APPLN. INFO.:			EP 2002-22540	20021007
			WO 2003-EP11073	20031007

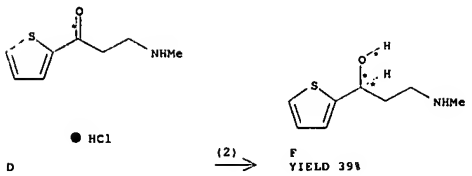
OTHER SOURCE(S): MARPAT 140:321232
GI



AB Title compds. (I, II; R1, R2 = H, alkyl, cycloalkyl, aralkyl, aryl), were prepared by reducing the corresponding 3-amino-1-(2-thienyl)-1-propanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and optionally a base. Thus, 3-N-methylamino-1-(2-thienyl)-1-propanone hydrochloride (preparation given) and NaOH were stirred 1 h in Me2CHOH; a prestirred solution of (1S,2R)-cis-1-amino-2-indanol and (p-cymene)ruthenium(II)chloride dimer in Me2CHOH was added followed by stirring for 4 h at 20° to give 39% (S)-N-methylamino-1-(2-thienyl)-1-propanol in 70% enantiomeric excess.

RX(2) OF 5 ...D ===> F

L6 ANSWER 5 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)



D F
YIELD 39%

RX(2)

STAGE(1)
CAT 126456-43-7 1H-Inden-2-ol, 1-amino-2,3-dihydro-, (1S,2R)-, 52462-29-0 Ruthenium, di-μ-chlorodichlorobis[(1,2,3,4,5,6-η)-1-methyl-4-(1-methylethyl)benzene]di-
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 20 minutes, 85 deg C
SUBSTAGE(2) 85 deg C -> 20 deg C

STAGE(2)
RCT D 645411-16-1
RGT G 1310-73-2 NaOH
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 1 hour, 20 deg C
SUBSTAGE(2) 20 deg C
SUBSTAGE(3) 4 hours, 20 deg C

PRO F 116539-55-0
NTE stereoselective

TI Preparation of optically active 3-amino-1-(2-thienyl)-1-propanols via reduction of 3-amino-1-(2-thienyl)-1-propanones using a hydrogen donor in the presence of a metal catalyst, an optically active nitrogen-containing ligand and optionally a base.
AB Title compds. (I, II; R1, R2 = H, alkyl, cycloalkyl, aralkyl, aryl), were prepared by reducing the corresponding 3-amino-1-(2-thienyl)-1-propanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and optionally a base. Thus, 3-N-methylamino-1-(2-thienyl)-1-propanone hydrochloride (preparation given) and NaOH were stirred 1 h in Me2CHOH; a prestirred solution of (1S,2R)-cis-1-amino-2-indanol and (p-cymene)ruthenium(II)chloride dimer in Me2CHOH was added followed by stirring for 4 h at 20° to give 39% (S)-N-methylamino-1-(2-thienyl)-1-propanol in 70% enantiomeric excess.
IT Reduction catalysts
(preparation of optically active aminothienylpropanols via reduction of aminothienylpropanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and a base)
IT Reduction
(stereoselective; preparation of optically active aminothienylpropanols via reduction of aminothienylpropanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and a base)
IT 7439-88-5D, Iridium, organometallic complexes 7440-16-6D, Rhodium, organometallic complexes 52462-29-0, (p-Cymene)ruthenium(II)chloride dimer 126456-43-7

L6 ANSWER 5 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
RL: CAT (Catalyst use); USES (Uses)
(prepn. of optically active aminothienylpropanols via redn. of aminothienylpropanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-contg. ligand and a base)
IT 116539-55-0P 132335-44-5P 625853-20-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of optically active aminothienylpropanols via reduction of aminothienylpropanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and a base)
IT 64-17-5, Ethanol, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of optically active aminothienylpropanols via reduction of aminothienylpropanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and a base)
IT 67-63-0, Isopropanol, reactions
RL: NUU (Other use, unclassified); RGT (Reagent); RACT (Reactant or reagent); USES (Uses)
(preparation of optically active aminothienylpropanols via reduction of aminothienylpropanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and a base)
IT 88-15-3, 2-Acetylthiophene 593-51-1, Methylamine hydrochloride 13196-35-5 18467-77-1, (-)-2,3:4,6-Di-O-isopropylidene-2-keto-L-gulonic acid 30525-89-4, Paraformaldehyde 114559-95-4, (+)-2,3:4,6-Di-O-isopropylidene-2-keto-D-gulonic acid 132335-48-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of optically active aminothienylpropanols via reduction of aminothienylpropanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and a base)
IT 569687-76-9P 645411-16-1P, 3-N-Methylamino-1-(2-thienyl)-1-propanone hydrochloride 679405-09-5P 679405-10-8P 679405-11-9P 679405-12-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of optically active aminothienylpropanols via reduction of aminothienylpropanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and a base)
IT 1310-58-3, Potassium hydroxide, reactions 1310-73-2, Sodium hydroxide, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of optically active aminothienylpropanols via reduction of aminothienylpropanones using a hydrogen donor in the presence of a metal catalyst, an optically active N-containing ligand and a base)

L6 ANSWER 6 OF 6 CASREACT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 140:253262 CASREACT
TITLE: Method for the preparation amino alcohols via the enantioselective hydrogenation of amino ketones
INVENTOR(S): Kralik, Joachim; Fabian, Kai; Muermann, Christoph; Schweickert, Norbert
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020389	A1	20040311	WO 2003-EP8513	20030801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2496883	AA	20040311	CA 2003-2496883	20030801
AU 2003260347	A1	20040319	AU 2003-260347	20030801
EP 1532100	A1	20050525	EP 2003-790842	20030801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013795	A	20050712	BR 2003-13795	20030801
CN 1678562	A	20051005	CN 2003-820304	20030801
JP 2005536556	T2	20051202	JP 2004-531845	20030801
US 2005261514	A1	20051124	US 2005-525821	20050225
ZA 2005002458	A	20051010	ZA 2005-2458	20050324

PRIORITY APPLN. INFO.: DE 2002-10240025 20020827
WO 2003-EP8513 20030801

OTHER SOURCE(S): MARPAT 140:253262
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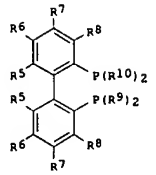
L6 ANSWER 6 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)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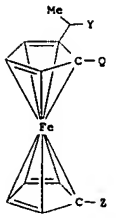
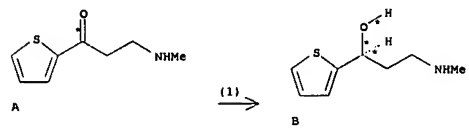

II

AB The invention relates to methods for the enantioselective production of amino alcs., R1CH(OH)CH2(CH2)nNHR2 [R1 = (un)substituted, (un)saturated or aromatic carbocycle or heterocycle (optionally substituted with R3, R4); R2 = H, C1-20-alkyl; R3, R4 = H, C1-20-alkyl, C1-20-alkoxy, aryl, aryloxy, CO2R2, F, Cl, Br, OH, CN,NO2,N(R2)2, NHCOR2; n = 0 - 3], via the enantioselective hydrogenation of amino ketones, R1COCH2(CH2)nNHR2 and is characterized by hydrogenation in the presence of a non-racemic catalyst containing a chiral diphosphine ligand I [R5, R6, R7, R8 = H, C1-20-alkyl, C1-20-alkoxy, aryl, aryloxy, F, Cl, Br,N(R2)2, NHCOR2; R5R6, R6R7, R7R8 = (CH2)4, CH:CHCH:CH,etc.; R9, R10 = C6H4(R11)m, 2-furyl, cyclohexyl; R11 = H, C1-20-alkyl, C1-20-alkoxy, aryl, aryloxy, SO3Na, COR12, F, Cl, N(R12)2, NHCOR12; R12 = H, C1-20-alkyl; m = 0 - 3] or II [Q = PPh2, P(cyclohexyl)2, P[C6H3(CF3)2-3,5], P(4-methoxy-3,5-dimethylphenyl)2, P(CMe3)2; Y = OH, P(cyclohexyl)2, P(C6H3Me2-3,5)2, P(CMe3)2; Z = H, PPh2; Ph = unsubstituted Ph, C6H4Me-2, C6H4Me-3, C6H4Me-4, C6H3Me2]. Thus, (S)-N-methyl-3-hydroxy-3-(2-thienyl)propanamine was prepared with 92.8% e.e. from 3-(methylamino)-1-(2-thienyl)-1-propanone via asym. hydrogenation in MeOH/PhMe containing catalytic bis(1,5-cyclooctadiene)dirhodium(I) dichloride and (S)-(-)-2,2'-bis[di(p-tolyl)phosphine]-1,1'-binaphthyl.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 2 A ===> B


A B

L6 ANSWER 6 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)

RX(1)

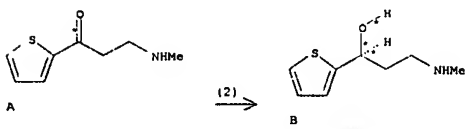
STAGE(1)
CAT 12092-47-6 Rh COD Cl dimer, 100165-88-6 Phosphine, (1S)-(1,1'-binaphthalene]-2,2'-diylbis[bis(4-methylphenyl)-
SOL 108-88-3 PhMe

STAGE(2)
RCT A 667465-15-8
SOL 67-56-1 MeOH

STAGE(3)
RGT C 1333-74-0 H2
CON 15 hours, 50 deg C, 55 bar

PRO B 116539-55-0
NTE stereoselective (92.8% e.e.); steel autoclave

RX(2) OF 2 A ===> B


A B
YIELD 94%

RX(2) RCT A 667465-15-8

STAGE(1)
RGT H 7727-37-9 N2
SOL 67-56-1 MeOH
CON 7 bar

STAGE(2)
CAT 12092-47-6 Rh COD Cl dimer, 76189-56-5 Phosphine, (1S)-(1,1'-binaphthalene]-2,2'-diylbis[diphenyl-
SOL 108-88-3 PhMe

STAGE(3)
RGT C 1333-74-0 H2
CON SUBSTAGE(1) 50 deg C, 10 bar
SUBSTAGE(2) 7 hours, 50 deg C, 120 bar

PRO B 116539-55-0
NTE stereoselective (98% e.e.); steel autoclave

TI Method for the preparation amino alcohols via the enantioselective hydrogenation of amino ketones

AB The invention relates to methods for the enantioselective production of amino alcs., R1CH(OH)CH2(CH2)nNHR2 [R1 = (un)substituted, (un)saturated or aromatic carbocycle or heterocycle (optionally substituted with R3, R4); R2 = H, C1-20-alkyl; R3, R4 = H, C1-20-alkyl, C1-20-alkoxy, aryl, aryloxy, CO2R2, F, Cl, Br, OH, CN,NO2,N(R2)2, NHCOR2; n = 0 - 3], via the enantioselective hydrogenation of amino ketones, R1COCH2(CH2)nNHR2 and is characterized by hydrogenation in the presence of a non-racemic catalyst contg. a chiral diphosphine ligand I [R5, R6, R7, R8 = H, C1-20-alkyl, C1-20-alkoxy, aryl, aryloxy, F, Cl, Br,N(R2)2, NHCOR2; R5R6, R6R7, R7R8 = (CH2)4, CH:CHCH:CH,etc.; R9, R10 = C6H4(R11)m, 2-furyl, cyclohexyl; R11 = H, C1-20-alkyl, C1-20-alkoxy, aryl, aryloxy, SO3Na, COR12, F, Cl, N(R12)2, NHCOR12; R12 = H, C1-20-alkyl; m = 0 - 3] or II [Q = PPh2, P(cyclohexyl)2, P[C6H3(CF3)2-3,5], P(4-methoxy-3,5-dimethylphenyl)2, P(CMe3)2; Y = OH, P(cyclohexyl)2, P(C6H3Me2-3,5)2, P(CMe3)2; Z = H, PPh2; Ph = unsubstituted Ph, C6H4Me-2, C6H4Me-3, C6H4Me-4, C6H3Me2]. Thus, (S)-N-methyl-3-hydroxy-3-(2-thienyl)propanamine was prepd. with 92.8% e.e. from 3-(methylamino)-1-(2-thienyl)-1-propanone via asym. hydrogenation in MeOH/PhMe contg. catalytic bis(1,5-cyclooctadiene)dirhodium(I) dichloride and (S)-(-)-2,2'-bis[di(p-tolyl)phosphine]-1,1'-binaphthyl.

ST amino alc chiral prepn; ketone amino enantioselective hydrogenation catalyst chiral phosphine ligand; binaphthyl chiral ligand enantioselective hydrogenation amino ketone; ferrocene chiral diphosphine ligand enantioselective hydrogenation amino ketone

IT Ketones, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(amino; preparation amino alcs. via the enantioselective hydrogenation of amino ketones with chiral diphosphine ligands)

IT Alcohols, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(amino; preparation amino alcs. via the enantioselective hydrogenation of amino ketones with chiral diphosphine ligands)

IT Ligands
RL: CAT (Catalyst use); USES (Uses)
(chiral, diphosphine; preparation amino alcs. via the enantioselective hydrogenation of amino ketones with chiral diphosphine ligands)

IT Amines, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(keto; preparation amino alcs. via the enantioselective hydrogenation of amino ketones with chiral diphosphine ligands)

IT Hydrogenation
Hydrogenation catalysts
(stereoselective; preparation amino alcs. via the enantioselective hydrogenation of amino ketones with chiral diphosphine ligands)

IT 76189-56-5, (S)-(-)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl 98327-87-8D, BINAP, axially chiral 100165-88-6, (S)-(-)-2,2'-Bis[di(p-tolyl)phosphino]-1,1'-binaphthyl 142293-39-8D, axially chiral 670218-73-2D, axially chiral 670218-74-3D, axially chiral
RL: CAT (Catalyst use); USES (Uses)
(chiral diphoshine ligand for enantioselective hydrogenation; preparation amino alcs. via the enantioselective hydrogenation of amino ketones with chiral diphosphine ligands)

IT 7439-88-5D, Iridium, complexes 7440-05-3D, Palladium, complexes 7440-16-6D, Rhodium, complexes 7440-18-8D, Ruthenium, complexes 12092-47-6, Bis[(1,5-cyclooctadiene)(chloro)rhodium)
RL: CAT (Catalyst use); USES (Uses)
(enantioselective hydrogenation catalyst; preparation amino alcs. via the enantioselective hydrogenation of amino ketones with chiral diphosphine ligands)

IT 27152-62-1, 3-(Methylamino)-1-phenyl-1-propanone 667465-15-8, 3-(Methylamino)-1-(2-thienyl)-1-propanone
RL: RCT (Reactant); RACT (Reactant or reagent)
(enantioselective hydrogenation of; preparation amino alcs. via the enantioselective hydrogenation of amino ketones with chiral diphosphine ligands)

L6 ANSWER 6 OF 6 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
IT 114133-37-8P, (S)-3-(Methylamino)-1-phenyl-1-propanol 116539-55-0P, (S)-3-(Methylamino)-1-(2-thienyl)-1-propanol
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation amino alcs. via the enantioselective hydrogenation of amino ketones with chiral diphosphine ligands)

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L5 MAY NOT BE USED HERE
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L7              2 L5 NOT L6

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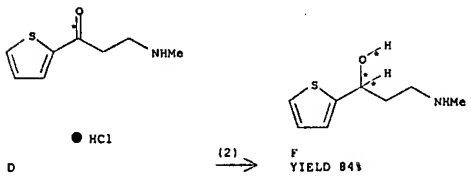
L7 ANSWER 1 OF 2 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:93915 CASREACT
TITLE: Process for the preparation of optically active 3-N-methylamino-1-(2-thienyl)-1-propanol
INVENTOR(S): Michel, Dominique
PATENT ASSIGNEE(S): Lonza A.-G., Switz.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005307	A1	20040115	WO 2003-EP7312	20030708
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003253036	A1	20040123	AU 2003-253036	20030708
PRIORITY APPLN. INFO.:			EP 2002-15161	20020709
			WO 2003-EP7312	20030708

OTHER SOURCE(S): MARPAT 140:93915
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(2) OF 4 ...D ===> F



D —(2)→ F
YIELD 84%

RX(2) RCT D 645411-16-1

STAGE(1)
RGT G 1310-73-2 NaOH, H 16940-66-2 NaBH4
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 5 minutes, 4 deg C
SUBSTAGE(2) 30 minutes, 4 deg C

L7 ANSWER 1 OF 2 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
SUBSTAGE(3) 4 hours, 4 deg C

STAGE(2)
SOL 67-64-1 Me2CO
CON SUBSTAGE(1) 5 minutes
SUBSTAGE(2) 10 minutes

STAGE(3)
SOL 7732-18-5 Water

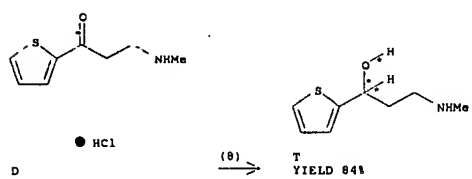
PRO F 116539-56-1

L7 ANSWER 2 OF 2 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:93914 CASREACT
TITLE: Process for the preparation of N-monosubstituted β-amino alcohols
INVENTOR(S): Michel, Dominique
PATENT ASSIGNEE(S): Lonza A.-G., Switz.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005239	A1	20040115	WO 2003-EP7411	20030709
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2491472	AA	20040115	CA 2003-2491472	20030709
AU 2003250924	A1	20040123	AU 2003-250924	20030709
BR 2003012651	A	20050426	BR 2003-12651	20030709
EP 1539673	A1	20050615	EP 2003-762669	20030709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1665773	A	20050907	CN 2003-816223	20030709
JP 2005532383	T2	20051027	JP 2004-518758	20030709
NO 2005000079	A	20050311	NO 2005-79	20050106
US 2005256318	A1	20051117	US 2005-520362	20050418
PRIORITY APPLN. INFO.:			EP 2002-15229	20020709
			WO 2003-EP7411	20030709

OTHER SOURCE(S): MARPAT 140:93914
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(8) OF 11 ...D ===> T



D —(8)→ T
YIELD 84%

RX(8) RCT D 645411-16-1

L7 ANSWER 2 OF 2 CASREACT COPYRIGHT 2006 ACS on STN (Continued)
STAGE(1)
RGT U 16940-66-2 NaBH4, V 1310-73-2 NaOH
SOL 7732-18-5 Water, 64-17-5 EtOH
CON SUBSTAGE(1) 5 minutes
SUBSTAGE(2) 30 minutes
SUBSTAGE(3) 4 hours

STAGE(2)
SOL 67-64-1 Me2CO
CON SUBSTAGE(1) 5 minutes
SUBSTAGE(2) 10 minutes

STAGE(3)
SOL 7732-18-5 Water

PRO T 116539-56-1